Lyme disease and Pregnancy
Epidemiology and Pathobiology of Borrelia:
Implications for Research

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Mom
Number of cases of notifiable vector-borne diseases in the U.S. in 2018, by disease

Number of cases of vector-borne disease U.S. 2018, by disease

Note(s): United States
Further information regarding this statistic can be found on page 8.
Source(s): CDC (NNDSS); ID 742326
“A lack of provider awareness of the absence of EM or nonclassical EM presentations can lead to underdiagnosis and delayed treatment, highlighting the need for better diagnostics for early LD.”

“Insufficiencies in current testing methodologies complicate the accurate diagnosis of early LD, contribute to delays in diagnosis and treatment, and may result in additional sequelae.”

The results obtained with this collection highlight and reinforce the known limitations of serologic testing in early LD, with only 29% of individuals presenting with EM lesion sizes of >5 cm yielding a positive result using the STTIA.
Pregnant women less often had a ring-like EM (42.4% vs. 55.3%, \( p = 0.002 \)), less often had EM located on the trunk (14.1% vs. 24.0%, \( p = 0.009 \)), and less often reported constitutional symptoms (22.4% vs. 37.2%, \( p < 0.001 \)).

“We do not have a reliable explanation for the observation that the pregnant women less often had ring-like EM despite similar duration of the skin lesion before treatment, but we stress that the findings in our control group are in agreement with previous reports.”

“Most manifestations of LB result from inflammation generated by the host immune response to the spirochete. Thus, fewer symptoms, as found in the present study of pregnant women with EM, may be associated with lower levels of inflammation.”
A recently released estimate based on insurance records suggests that each year approximately 476,000 Americans are diagnosed and treated for Lyme disease. This number is likely an over-estimate of actual infections because patients are sometimes treated presumptively in medical practice. Regardless, this number indicates a large burden on the health care system and the need for more effective prevention measures.

“A recently released estimate based on insurance records suggests that each year approximately 476,000 Americans are diagnosed and treated for Lyme disease.”
Comparing Annual Cases of STDs to Lyme disease

Considerations

- Case numbers of other vector-borne diseases show that ticks are not great vectors.
- Distribution of vectors in US:
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4844559/
- Data strongly suggests other routes of transmission
- Data also suggests humans have become reservoir hosts

https://www.cdc.gov/nchs/hus/contents2019.htm#Table-010
“Despite the fact that some authors consider that antibiotic therapy of a pregnant mother diagnosed with Lyme disease allows normal development of the child (Walsh et al. 2007, Leslein 2010), it must be kept in mind that the treatment of Lyme disease is sometimes long and difficult (Embers et al. 2012). The ability of long-term survival of B. burgdorferi in tissues and spreading of spirochetes in the body despite antibiotic treatment can contribute to intergenerational infection of Lyme disease.”
<table>
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<th>Animal Studies Showing Vertical Transmission of <em>Borrelia burgdorferi</em></th>
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“It is possible that non-arthropod transmission could introduce the spirochete into populations outside of the geographical range of the tick vector. The apparent ease by which organisms can be transmitted by these mechanisms demands closer inspection if the overall epidemiologic and epizootiologic picture is to be understood.” – Gustafsen, 1993

“If fetuses can be infected in-utero with B. burgdorferi, as suggested by Anderson et al. (1987), and if they can survive transplacental transmission, this may be a means of maintaining the spirochete in the rodent population in the absence of ticks.” – Burgess, 1993

“… these results indicated that B. burgdorferi can transmit by other modes than the tick bite.” – Altaie et al, 1996

“This could mean that a survey for Bb infection using the presence of antibodies alone as the method of detection may underestimate the prevalence of infection.” – Burgess et al, 1989.

“Intrauterine infection by B. burgdorferi does occur in dogs and is a potential means by which the spirochete can be transmitted in a breeding population in the absence of a tick vector.” – Gustafson et al, 1993

“The findings of this study of natural B. burgdorferi infection in pregnant dairy heifers supports previous observations of both natural and experimental in-utero infections with B. burgdorferi in domestic animals and give further evidence of B. burgdorferi occurs during gestation in naturally infected cattle.” – Bushmich et al, 1998

“Vertical transmission of B. burgdorferi was confirmed with B. burdorferi isolated from foetuses of Apodemus agrarius and Rattus edwardsi. The results showed that Lyme disease spirochetes might be naturally maintained in an enzootic cycle by transplacental transmission.” - Wan et al, 1999.
Are there other ways to get Lyme disease?

- “Untreated Lyme disease during pregnancy can lead to infection of the placenta. Spread from mother to fetus is possible but rare.
- Fortunately, with appropriate antibiotic treatment, there is no increased risk of adverse birth outcomes.
- There are no published studies assessing developmental outcomes of children whose mothers acquired Lyme disease during pregnancy.”

Current Trends Update: Lyme Disease and Cases Occurring during Pregnancy -- United States

MMWR June 28, 1985 / 34(25);376-8,383-4

“…CDC have established a registry to enroll cases of Lyme disease in pregnant women before the outcome of pregnancy is known. Of the 19 pregnancies evaluated to date, none resulted in a child with a congenital heart defect. However, other adverse outcomes were found, including intrauterine fetal demise in the second trimester, prematurity, and developmental delay with cortical blindness. None of the adverse outcomes have been documented to be caused by Lyme disease. Outcomes of 14 of the pregnancies were completely normal. The risk of adverse outcome for pregnancies complicated by Lyme disease is not currently known.

5 of 19 (26%) pregnancies had adverse outcomes
Adverse fetal outcomes in pregnant moms with Lyme disease

“…appraised by fetal loss and stillbirth, pre-term birth, offspring malformations…”

2010

“Adverse outcomes” in 12% of IV treated moms; 31.6% of oral treated moms; and 60% of untreated moms

2018

“Adverse outcomes” in 11% of treated moms and 50% of untreated moms

2020

“Adverse outcomes” in 14% of IV treated moms. All pregnant moms were treated
The outcome of pregnancy was unfavorable in 42/304 (13.8%) of TREATED patients.

- Preterm birth in 22/42 (52.4%)
- Fetal/perinatal death in 10/42 (23.8%)
- Anomalies in 15/42 (35.7%).
Several spirochetes are known to cause transplacental infections in animals and humans. *T. pallidum* is the spirochete that has been the most known to cause congenital infection in humans. Adverse fetal outcomes have also been reported in gestational infections with *Leptospira canicola*, the etiologic agent of leptospirosis, and with *Borrelia* species including *Borrelia recurrentis*, the etiologic agent of relapsing fever (6). *B. burgdorferi* is a spirochete, thus congenital infection could be predicted.

• Lack of prenatal care and gaps in testing and treatment among those who do receive prenatal care are significant challenges for preventing congenital syphilis.
• Even among those receiving some prenatal care, the detection and treatment of maternal syphilis often occurs too late in pregnancy to prevent congenital syphilis.
Borrelia miyamatoi is a “relapsing fever” strain transmitted by the same ticks that transmit Lyme disease.
• Transplacental transmission of the human fetus has been recognized for **relapsing fever borreliosis** as well as Lyme disease...

• Gestational tick-borne disease can be transmitted to unborn children in-utero and **has the potential to cause premature labor and fetal death.**

• Hormonal changes during pregnancy can **lead to changes in immune function** that may affect detection of clinical or laboratory findings.
“Further evaluation of non-tick bite transmission of Lyme disease, for example maternal-fetal transmission.”

“It is surprising that the evidence presented for transplacental transmission has received little notice by investigators. It would seem that the clinical and epidemiological implications, if significant, could have an impact on current thinking and measures taken to manage the disease.”